REMARKS

Claims 113-119 and 134 are pending in this application. Claim 113 is amended for clarity to recite that "...the solution comprises at least one of salts, alcohols, polyols, amino acids, sugars, proteins, polysaccharides, aqueous solutions thereof, and a mixture thereof..." and "...the physically crosslinked polymer hydrogel is formed by controlling the gelation rate by changing Flory Interaction parameter of the solution from a lower to a higher value...." Claims 113 and 114 are amended for clarity to recite that "...the physically crosslinked polymer hydrogel is formed by controlling the gelation rate by changing Flory Interaction parameter of the solution from a lower to a higher value...." Amendments are fully supported by the specification (see paragraphs [0014], [0021], [0022], [0023], [0030], [0055], [0111], and [0241] for example. Claim 134 is new and is fully supported by the specification (see paragraphs [0020], [0030], [0031], and [0057] of the published application, for example). Therefore no new matter is introduced. The Office Action is discussed below:

Anticipation/Obviousness Rejections and the Examiner's Response to Arguments:

On pages 2-3 of the Office Action, the examiner has maintained the rejection of claim 113 allegedly as being anticipated by Hyon (US 4,663,358) or Yamauchi (JP 03215417).

On pages 2-3 of the Office Action, the examiner also has maintained the rejection of claims 113-119 allegedly as being anticipated by or, in the alternative, as being obvious over Tanihara (US 5,880,216), Ku (US 5,981,826), Yao (US 6,268,405), or Okamura (JP 04338326).

Regarding the response filed July 30, 2007, the examiner asserts that the arguments filed regarding Hyon *et al.*, Ku *et al.*, Yao *et al.* and Okamura are not persuasive. Applicants disagree with the examiner and indicate that examiner has failed to understand the patentable novelty clarified in the response and the distinctions made of the claimed invention over the cited references.

Regarding Hyon *et al.*, Ku *et al.*, Yao *et al.*, Okamura and Tanihara *et al.*, the patentable novelty of the claims over these arts is that "the physically cross-linked hydrogel is formed without chemical cross-linkers, irradiation or thermal cycling", which is clearly recited in the claims. Applicants, reiterate, however, the examiner has not comprehended the distinction made therein.

In addition, applicants point out that Ku, Yao, Hyon, and Okamura all require freezing step to form a hydrogel. This statement is supported in Ku *et al.* (see claim 1), Yao (see claim 1), Hyon (see claim 1) and Okamura (see the "constitution"). Applicants also point out, Yamauchi *et al.* states in the constitution that ionized radiation is used to form a gel. Therefore, to achieve a hydrogel by following Yamauchi, the body cavity would have to be subjected to ionizing radiation, reduced in temperature below 0ºC, or have additional chemical reactants added to it in order for the liquid material introduced into the cavity to form a hydrogel. Applicants clarify that the instant invention requires no such further steps, which is further evidenced by the declaration submitted herewith (see Figure 2, Tests 1-4, for example).

Regarding how the amendments avoid such references or objections, applicants indicate that the amended claims recite "injectable solution for injection into a body cavity" and "the solution of the polymer hydrogel gels *in situ* after the injection", which clearly distinguish the claims from the cited references or any combination of the cited references. Applicants also indicate that none of the cited references or any combination thereof provide "an injectable solution for injection into a body cavity", wherein the "hydrogel is formed without chemical cross-linkers, irradiation or thermal cycling", and the "hydrogel gels *in situ* after the injection", which is further supported by the experimental results as shown in the declaration submitted herewith (see for example, Figure 2, Tests 1-4).

Regarding Tanihara *et al.*, contrary to the arguments filed on July 30, 2007, the examiner contends that a PVA polymer need not be majority -CH2-CHOH-. The examiner believes that even a copolymer of vinyl alcohol, for derivitazation of some units or from copolymerization, is a generic PVA polymer. The examiner also believes that a copolymer is only a type of polymer and still a polymer and within the scope of

the claims. The examiner asserts that the exclusion of PVA copolymers is not required in the rejected claim(s). Applicants disagree with the examiner and believe that the examiner has failed to understand the distinction that the "PVA" disclosed by Tanihara contains structural units at mole fractions of 0.05 to 0.5 of the formula I and/or formula II in that patent, and is thus termed a 'copolymer', and cannot be simply described as "PVA" (see Tanihara col. 3, line 64 through col. 4, line 21).

Applicants reiterate that Tanihara *et al.* disclosure is not relevant to the claimed invention, because they do not describe a PVA hydrogel for the reasons clarified above and in the response to the previous Office Action filed on March 2, 2007 and July 30, 2007. Applicants further point out that the material described by Tanihara is not a PVA polymer (see accompanying Declaration of Dr. Spiegelberg, section 5), and rather a molecule with a specific pendant group (see Tanihara, formula I, for example). Therefore, Tanihara disclosure is not relevant to the claimed invention.

Applicants, further point out that Tanihara itself appears to make this distinction (see comparative example 1) by requiring a separation between PVA and a PVA with a new pendant group. The basic PVA is proven by Tanihara not to gel under the conditions described therein, whereas instant invention discloses methods to render it gellable. A further distinction between the "PVA" of Tanihara and the PVA described in the instant disclosure is that the gels of the Tanihara are shown to be resistant to high temperatures in excess of 100°C (see column 21, line 4), which indicates that the cross-linking is either chemical or does not involve physically cross-linked hydrated PVA crystals (*see* Peppas, N.A. & Stauffer, S. R., "Reinforced uncrosslinked poly (vinyl alcohol) gels produced by cyclic freezing-thawing processes: a short review," *Journal of Controlled Release*, 16 (1991) 305-310; Peppas, N. A. *et al.*, "Physicochemical Foundations and Structural Design of Hydrogels in Medicine and Biology," Annu. Rev. Biomed. Eng., 02:9-20, 2000; and US Patent No. 7,235,592). Applicants refer to the declaration of Dr. Spiegelberg (see enclosed declaration, Test 3, for example), which proves that physically cross-linked hydrogels melt at temperatures below boiling water. However, applicants also point out that in order to get a hydrogel from the starting material Tanihara *et al.* used one of (1) cross-linking with radiation or peroxides; (2)

cooling the solution; (3) freezing of the solution; and (4) repetition of freezing and thawing (see column 20, line 15). In additional, Tanihara methods require either chemical reaction of the polymer solution with an anhydride or taurine, or a freeze-thaw process. In contrast, the claimed invention requires none of these steps.

Regarding the injectability of the prior art hydrogels, the examiner contends that the experiment as described in the declaration (filed March 2, 2007) was not commensurate in scope with what is actually being claimed. In order to address the issue and to demonstrate that the none of the processes disclosed in the cited references yield "injectable hydrogel", applicant herewith submit a declaration of Dr. Stephen Spiegelberg, which is based on additional four experiments, which demonstrate that the claimed materials are injectable and spontaneously form gel after injection. The experiments also provide, on the contrary, the proof that the materials disclosed in the cited arts are not injectable. The data also support the claimed invention that the polymer hydrogel gels *in situ* after the injection without a further processing step. This is not possible using chemical cross-linking, radiation cross-linking, or thermal processing techniques to create the gels disclosed in the cited references (see attached Declaration, Tests 1-4, for example).

The examiner further asserts that the prior art final product need not correspond with the claimed final product. According to the examiner, if the intermediate product in the prior art meets the compositional requirements for applicant's product, then the requirements to reject that composition claims are met and they are unpatentable over the prior art. Applicants disagree with the examiner and indicate that the examiner's interpretation of the intermediate product as the claimed final product is not applicable in this case, because, the physicochemical properties (for example, the injectability) of claimed final product is critical and required, otherwise the claimed product would not be usable as recited in the claims. In addition, applicants indicate that if an intermediate of the claimed final product is "injectable", would not be useful unless the final product also is "injectable" as the claimed product is directed to the application recited in the claims that the claimed injectable hydrogel is "for injection into a body cavity" and "gels *in situ* after the injection."

In this regard, applicants refer the examiner to the dictates of the MPEP that:

> "IF PRIOR ART COMPOUNDS HAVE NO UTILITY, OR UTILITY ONLY AS INTERMEDIATES, CLAIMED STRUCTURALLY SIMILAR COMPOUNDS MAY NOT BE *PRIMA FACIE* OBVIOUS OVER THE PRIOR ART
>
> If the prior art does not teach any specific or significant utility for the disclosed compounds, then the prior art is not sufficient to render structurally similar claims *prima facie* obvious because there is no motivation for one of ordinary skill in the art to make the reference compounds, much less any structurally related compounds. *In re Stemniski*, 444 F.2d 581, 170 USPQ 343 (CCPA 1971).
>
> Where structurally similar "prior art compounds 'cannot be regarded as useful' for the sole use disclosed [by the reference],... a person having ordinary skill in the art would lack the 'necessary impetus' to make the claimed compounds." *In re Albrecht*, 514 F.2d 1389, 1396, 185 USPQ 585, 590 (CCPA 1975) ....
>
> Similarly, if the prior art merely discloses compounds as intermediates in the production of a final product, one of ordinary skill in the art would not have been motivated to stop the reference synthesis and investigate the intermediate compounds with an expectation of arriving at claimed compounds which have different uses. *In re Lalu*, 747 F.2d 703, 223 USPQ 1257 (Fed. Cir. 1984)." (Emphasis added).

See MPEP § 2144.09 (Rev. 6, September 2007 at 2100-161-162).

Therefore, contrary to the examiner's speculation, even if an intermediate product in a prior art meets the compositional requirements for a claimed product, the requirements to reject that composition claims are not met, because the intermediate product of the cited references is not retainable as the claimed final product and not usable as recited in the claims.

Applicants also refer the examiner to the MPEP that:

> "Rebuttal evidence may include evidence of "secondary considerations," such as "commercial success, long felt but unsolved needs, [and] failure of others." *Graham v. John Deere Co.*, 383 U.S. at 17, 148 USPQ at 467. See also, e.g., *In re Piasecki*, 745 F.2d 1468, 1473, 223 USPQ 785, 788 (Fed. Cir. 1984) (commercial success). Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art."

See MPEP § 2145 (Rev. 6, September 2007 at 2100-162-163).

In this regard applicants refer to the attached declaration (see section 3, for example) that the resulting unexpectedly improved properties of the claimed invention/product has fulfilled long felt but unsolved needs.

Without acquiescing in the rejection, in order to expedite the prosecution, for clarity, and to further distinguish the claimed invention from the cited references, applicants amend claim 113 to recite that "...the solution comprises at least one of salts, alcohols, polyols, amino acids, sugars, proteins, polysaccharides, aqueous solutions thereof, and a mixture thereof..." and "...the physically crosslinked polymer hydrogel is formed by controlling the gelation rate by changing Flory Interaction parameter of the solution from a lower to a higher value..." and amend claims 113 and 114 to recite that "...the physically crosslinked polymer hydrogel is formed by controlling the gelation rate by changing Flory Interaction parameter of the solution from a lower to a higher value...." Support for the amendments can be found throughout the specification, (see paragraphs [0014], [0021], [0022], [0023], [0030], [0055], [0111], and [0241] of the published application, for example).

In view of the above clarifications, amendments, arguments, attached declaration and the response of the record, withdrawal of the alleged anticipation/obviousness rejection is solicited.

REQUEST

Applicants submit that claims 113-119 and 134 are in condition for allowance and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,

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Date

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